REMARKS

Entry of the foregoing and further and favorable consideration of the subject application, in light of the following remarks, are respectfully requested.

As correctly stated in the Official Action, Claims 1, 4, and 24-33 are pending in the present application. Claims 1, 4, and 24-33 stand rejected.

By the present amendment, independent Claims 1 and 32 have been amended to recite that the candidate subject has "signs of aging of the skin." These amendments are supported, at least, by page 1, line 30. Claim 27 has been amended to correct a typographical error. New Claims 34-42 have been added, mirroring current Claims 4 and 24-31, but depending from independent Claim 32. No new matter has been added.

Rejections Under 35 U.S.C. § 102(b)

Claims 1, 4, and 24-31 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lee (U.S. Patent Nos. 5,132,119; 5,552,162; or 5,569,678). This rejection is respectfully traversed.

In order to anticipate a claim under 35 U.S.C. § 102, a reference must disclose or suggest each and every element of the claimed invention. Initially, Applicants note that independent Claim 1 recites that the regime or regimen comprises administering a calcium channel blocker to a candidate subject with signs of aging of the skin in need of such regime or regimen. Applicants respectfully submit that Lee et al. do not disclose or suggest each and every element of the presently claimed invention.

All three Lee patents are directed towards methods of preventing or treating scar tissue. Applicants note that the disclosures of the three Lee patents are relatively similar; for ease of reference, Applicants refer mainly to the Lee '678 patent previously cited by the Examiner. Applicants respectfully submit that the candidate subjects of the presently claimed invention and that of Lee et al. are different. The presently claimed invention is aimed at loosening and/or relaxing cutaneous and/or subcutaneous skin tissue via contractile fiber decontraction or relaxation. Thus, the subject in need of such treatment is **one with signs of aging of the skin** who requires contractile fiber decontraction/relaxation to smooth the skin. The subject of Lee et al. does not require contractile fiber decontraction/relaxation, but rather is afflicted with scars and requires the modulation of collagen biosynthesis. Accordingly, the subject populations of the presently claimed invention and Lee et al. are not the same. The Federal Circuit has held that the limitations concerning the subject being treated are relevant to the determination of the scope and meaning of a method of treatment claim. *See, e.g., Jansen v. Rexall Sundown Inc.*, 68 U.S.P.Q.2d 1154, 1158 (Fed. Cir. 2003); *Rapoport v. Dement*, 59 U.S.P.Q.2d 1215 (Fed. Cir. 2001). Copies of these decisions are enclosed for the Examiner's convenience. In particular, Applicants note that in *Rapoport*, the court explicitly rejected inherency arguments similar to those found in the current Office Action. *See Rapoport* at 1222. One practicing the methods disclosed by Lee et al. would not inherently be practicing the presently claimed invention, nor *vice versa*.

For example, Lee '678 discloses the prevention or treatment of scar tissue, by using a calcium channel inhibitor that controls the molecular (collagen and proteoglycan secretion) and cellular (fibroblast synthesis and cell shape) aspects of

the scarring process (cf. col. 4, lines 1-41). The consecutive change toward matrix degradation gives a softened and faded scar tissue; however, there is no mention of any action on contraction/relaxation mechanism nor any specific effects of "loosening and/or relaxing" skin tissue, the object of the presently claimed invention. The scar tissue of Lee et al. is damaged skin tissue with molecular and cellular specificities (col. 1 and col. 4: growth factors, over-secretion of proteins and collagen) that are not shared by normal skin tissue. Accordingly, there is no evidence that a calcium channel inhibitor would have the same effect on both of these tissue types.

Contractile fiber decontraction or relaxation is disclosed or suggested nowhere in any of the Lee et al. publications. Lee et al. cite the overproduction of protein and collagen as leading to excessive scarring or keloid formation. (Col. 4, lines 21-25). In contrast, mechanisms such as contractile fiber decontraction or relaxation underlie the loosening and/or relaxing of cutaneous or subcutaneous tissue in the presently claimed invention. Thus, the purpose of Lee et al. is to prevent molecular and/or cellular disorders due to injury rather than utilizing the mechanical process of contractile fiber decontraction or relaxation. The end results of Lee et al. described in Example 5 are a softening and fading of scars, disappearance of scar contracture, reduction in scar size and shrinkage of scars. (Col. 12, lines 5-24). In particular, Applicants respectfully submit that the effects of a reduction in scar size and shrinkage of scars directly contrast with the claimed invention which achieves a loosening and/or relaxing effect on cutaneous and/or subcutaneous tissue.

Lee et al. disclose that calcium channel antagonists are able to regulate cell shape, in particular, fibroblast shape (col. 4, Lee et al.), and viability of the cell.

However, Lee et al. do not disclose that these features correlate with "smoothing of the skin," which the present specification shows is a result of a regulation of the contraction/relaxation mechanism of the underlying contractile fibers in cutaneous and subcutaneous tissue. Applicants respectfully point out that the microrelief of the skin is defined by micro-depressions on the surface of the skin, generated by fiber contraction phenomena.

Additionally, Applicants respectfully point out that the existence of calcium channels inside cutaneous and subcutaneous skin tissue was not determined until 1999 as disclosed in the specification on page 6, lines 9-11. Thus, neither Lee et al. nor one skilled in the art could have envisioned that the presently claimed invention was even possible in 1989, 1993, or 1994 when Lee et al. filed their respective applications. Accordingly, one skilled in the art would not have been motivated to apply the calcium antagonists to non-scarred tissue, *i.e.*, cutaneous and/or subcutaneous tissue in need of loosening and/or relaxation. Thus, the presently claimed invention is not disclosed or even suggested by Lee et al.

Therefore, Applicants respectfully submit that Lee et al. cannot anticipate the presently claimed invention. Withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 32-33 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Lee et al. ('119, '162, and '678 patents) in view of De Lacharriere et al. (U.S. Patent No. 5,869,068). This rejection is respectfully traversed.

To establish a case of *prima facie* obviousness under 35 U.S.C. § 103, a reference or group of references must 1) disclose or suggest motivation to modify

the reference or combine reference teachings, 2) provide a reasonable expectation of success, and 3) disclose or suggest each and every element of the claimed invention. As is true for independent Claim 1 discussed above, independent Claim 32 recites that the regime or regimen comprises administering a calcium channel blocker to a candidate subject with signs of ageing of the skin in need of such regime or regimen. Applicants have already noted the deficiencies of the Lee et al. patents above with regard to the failure to disclose or suggest the administration of a calcium channel blocker to a candidate subject with signs of aging of the skin. This deficiency is not remedied by De Lacharriere et al.

Furthermore, as noted above, Lee et al. is directed to wound healing. In contrast, De Lacharriere et al. is concerned with wrinkles. Moreover, De Lacharriere et al. uses chlorine channel agonists, wherein Lee et al. use calcium channel blockers. Thus, there is no motivation to combine the disclosures of Lee et al. and De Lacharriere et al. because they are directed to two completely different endeavors and the use of two different mechanisms of action.

Applicants note that the Office Action incorrectly interpreted De Lacharriere et al. as using chlorine channel blockers. In fact, De Lacharriere et al. use chlorine channel agonists, *i.e.*, activators of chlorine channels, not blockers. *See, e.g.*, abstract; col. 2, ll. 55-64.

Neither Lee et al. nor De Lacharriere et al., either alone or in combination disclose or suggest each and every element of the presently claimed invention. Additionally, there is no motivation to combine these publications. Therefore, the Lee et al. and De Lacharriere et al. publications cannot anticipate the presently claimed invention. Withdrawal of this rejection is respectfully requested.

Double Patenting

Claims 1, 4, and 24-33 stand rejected under the judicially created doctrine of obviousness-type double patenting as purportedly unpatentable over Claims 1-11 of U.S. Patent 6,344,461, either alone, or in view of De Lacharriere et al. Without conceding to the merits of this rejection, and solely in an effort to expedite prosecution, Applicants submit herewith a terminal disclaimer over the '461 patent. Withdrawal of this rejection is respectfully requested.

Conclusions

From the foregoing, further and favorable consideration of the subject application in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

If there are any questions concerning this amendment, or the application in general, the Examiner is respectfully requested to telephone Applicants' undersigned representative so that prosecution may be expedited.

Respectfully submitted,

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Date: April 21, 2004

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